PSJ14 Janssen Opp Exh 22 – JAN-MS-00238335

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAR 5 1998

TRANSMITTED VIA FACSIMILE

Jacqueline Brown
Regulatory Affairs
Janssen Pharmaceutica
P.O. Box 200
Titusville, NJ 08560-0200

Re: NDA 19-813
Duragesic (fentanyl transdermal system)
MACMIS File ID #6194

Dear Ms. Brown:

This letter is in reference to Janssen Pharmaceutica's (Janssen) submission dated November 17, 1997, of promotional materials under cover of Form FDA 2253 for Duragesic (fentanyl transdermal system). This submission consists of three different convention posters (DR309A, B, C). The Division of Drug Marketing, Advertising, and Communications (DDMAC) regards these materials to be false or misleading. The dissemination of these posters is in violation of the Federal Food, Drug, and Cosmetic Act and the regulations promulgated thereunder. Our specific objections to the information presented in these posters are presented below:

Misleading Comparisons to Competitive Agents

Promotional poster DR309 B disseminated by Janssen makes claims that Duragesic caused significantly less constipation than morphine. Janssen combines the statement that "[t]he constipation got so bad, I was afraid to swallow my pain pills ..." with a bar chart comparing the incidence of constipation reported in an open cross-over clinical trial by Ahmedzai and Brooks[1] that compared fentanyl transdermal system with sustained-release morphine in the treatment of cancer pain to imply that fentanyl transdermal system is superior to sustained-release oral morphine. However, claims of superiority to other competitive drug products require substantial evidence. DDMAC has considered substantial evidence generally, to consist of two adequate and well-controlled, head-to-head studies of the drugs. DDMAC does not consider the study by Ahmedzai and Brooks to constitute substantial evidence.

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1 Sam Ahmedzai and David Brooks, *Transdermal Fentanyl versus Sustained-Release Oral Morphine in Cancer Pain: Preference, Efficacy, and Quality of Life*, Journal of Pain and Symptom Management, May 1997, 254, 261.

The poster DR309 C presents the statement that "I needed the relief the pain pills gave me, but the constipation kept me from doing the things I wanted to do..." with the claim that "Duragesic provides less frequency and impact of side effects." The combination of these statements imply that Duragesic is superior to sustained-release oral morphine. As noted previously, such superiority claims require substantial evidence.

Janssen also selectively presents the results of the Ahmedzai and Brooks study to provide the misleading impression that the tolerability profile of fentanyl transdermal system is superior to sustained-release morphine. In poster DR309 B, as noted previously, Janssen states that "Duragesic provided significantly less constipation than morphine." However, Janssen fails to present data from the Ahmedzai and Brooks study that the fentanyl group reported greater number of sleep disturbances and shorter duration of sleep than were reported with sustained-release oral morphine. Additionally, Janssen failed to disclose that the incidence of abdominal pain, dyspnea, and sweating were markedly higher with the use of fentanyl transdermal system and that more patients required rescue medication with the use of Duragesic than with the use of sustained-release oral morphine.

Promotion of Unapproved Use

In all three posters, Janssen presents in bold type across the top of the poster that the fentanyl transdermal system is recommended for use in chronic pain. However, the approved product labeling states the drug is "indicated in the management of chronic pain in patients who require continuous opioid analgesia for pain that cannot be managed by lesser means ...."

DDMAC considers the presentation of the full indication near the bottom of the poster in small, inconspicuous type size, misleading and overwhelmed by the more prominent claim of chronic pain at the top of the poster. Therefore, DDMAC considers Janssen to be promoting Duragesic for a much broader use than that recommended in the approved product labeling.

False or Misleading Statements

Janssen states that Duragesic "[s]tops the pain. Not the patient," indicating that fentanyl transdermal patch is not associated with impairment of mental or physical abilities. However, the approved product labeling contains a precaution that the use of strong opioid analgesics impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving and that patients given Duragesic should not drive unless tolerant to the effects of the drug. Janssen's statement implies that the use of Duragesic is not associated with any impairment of mental or physical abilities. Janssen has not submitted data to substantiate such a

claim. DDMAC considers the use of this statement to imply that the use of Duragesic is not associated with the impairment of mental or physical capabilities to be false or misleading.

Additionally, the presentation of statements concerning the incidence of constipation associated with the use of other opioid analgesics suggests that the use of Duragesic is not associated with constipation. The approved product labeling states that the use of Duragesic is associated with constipation. Suggestions that the use of Duragesic is not associated with constipation are false or misleading.

Fair Balance

DDMAC notes that the risk information on each of these posters is not presented with a prominence and readability comparable to the claims of efficacy. The presentation of the efficacy statements are presented in large type size that is easily readable. This presentation is contrasted to the single line of information concerning the risks associated with the use of Duragesic presented in small type size near the bottom of the poster that is difficult to detect and to read. Therefore, these posters are considered to be lacking in fair balance or otherwise misleading.

Janssen should immediately suspend all promotional activities and materials that convey or contain the allegedly violative claims or information identified in this letter until these allegations are resolved. Janssen should submit a written response to DDMAC on or before March 20, 1998, listing all the promotional materials that contain the same or similar violative promotional claims and when the use of these violative materials will be or has been discontinued.

Janssen should address any correspondence or additional questions to the undersigned at the Division of Drug Marketing, Advertising, and Communications, HFD-40, Rm 17 B-17, 5600 Fishers Lane, Rockville, Maryland 20857. DDMAC reminds Janssen that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS ID #6194, in addition to the NDA number.

Sincerely,

Stephen W. Sherman
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications